Clinical Topics

Diagnosis of brain death

Statement issued by the honorary secretary of the Conference of Medical Royal Colleges and their Faculties in the United Kingdom on 11 October 1976

British Medical Journal, 1976, **2**, 1187-1188

With the development of intensive care techniques and their wide availability in the United Kingdom it has become commonplace for hospitals to have deeply comatose and unresponsive patients with severe brain damage who are maintained on artificial respiration by means of mechanical ventilators.

This state has been recognised for many years and it has been the concern of the medical profession to establish diagnostic criteria of such rigour that on their fulfilment the mechanical ventilator can be switched off, in the secure knowledge that there is no possible chance of recovery.

There has been much philosophical argument about the diagnosis of death, which has throughout history been accepted as having occurred when the vital functions of respiration and circulation have ceased. With the technical ability to maintain these functions artificially, however, the dilemma of when to switch off the ventilator has been the subject of much public interest. It is agreed that permanent functional death of the brain stem constitutes brain death and that once this has occurred further artificial support is fruitless and should be withdrawn. It is good medical practice to recognise when brain death has occurred and to act accordingly, sparing relatives from the further emotional trauma of sterile hope.

Codes of practice, such as the Harvard criteria,[1] have been devised to guide medical practitioners in the diagnosis of brain death. These have provided considerable help with the problem and they have been refined as the knowledge gained from experience has been collated. More recently Forrester has written on established practice in Scotland[2] and Jennett has made useful observations.[3]

The diagnostic criteria presented for brain death here have been written with the advice of the subcommittee of the Transplant Advisory Panel, the working party of the Royal College of Physicians, and the working party of the Faculty of Anaesthetists and the Royal College of Surgeons and have been approved by the Conference of Medical Royal Colleges and their Faculties in the United Kingdom. They are accepted as being sufficient to distinguish between those patients who retain the functional capacity to have a chance of even partial recovery from those in whom no such possibility exists.

Conditions for considering diagnosis of brain death

All of the following should coexist.

(1) *The patient is deeply comatose.*

(*a*) There should be no suspicion that this state is due to depressant drugs. Narcotics, hypnotics, and tranquillisers may have prolonged durations of action, particularly when some hypothermia exists. The benzodiazepines act cumulatively and their effects persist, and they are commonly used as anticonvulsants or to assist synchronisation with mechanical ventilators. It is therefore recommended that the drug history should be carefully reviewed and adequate intervals allowed for the persistence of drug effects to be excluded. This is of particular importance in patients whose primary cause of coma lies in the toxic effects of drugs followed by anoxic cerebral damage.

(*b*) Primary hypothermia as a cause of coma should have been excluded.

(*c*) Metabolic and endocrine disturbances that can cause or contribute to coma should have been excluded. Metabolic and endocrine factors contributing to the persistence of coma must be carefully assessed. There should be no profound abnormality of the serum electrolytes, acid base balance, or blood glucose concentrations.

(2) *The patient is being maintained on a ventilator because spontaneous respiration had previously become inadequate or had ceased altogether.*

Relaxants (neuromuscular blocking agents) and other drugs should have been excluded as a cause of respiratory inadequacy or failure. Immobility, unresponsiveness, and lack of spontaneous respiration may be due to the use of neuromuscular blocking drugs, and the persistence of their effects should be excluded by eliciting spinal reflexes (flexion or stretch) or by showing adequate neuromuscular conduction with a conventional nerve stimulator. Equally, persistent effects of hypnotics and narcotics should be excluded as the cause of respiratory failure.

(3) *There should be no doubt that the patient's condition is due to irremediable structural brain damage. The diagnosis of a disorder which can lead to brain death should have been fully established.*

It may be obvious within hours of a primary intracranial event such as severe head injury, spontaneous intracranial haemorrhage, or after neurosurgery that the condition is irremediable. But when a patient has suffered primarily from cardiac arrest, hypoxia, or severe circulatory insufficiency with an indefinite period of cerebral anoxia or is suspected of having cerebral air or fat embolism then it may take much longer to establish the diagnosis and to be confident of the prognosis. In some patients the primary condition may be a matter of doubt and a confident diagnosis may be reached only by continuous clinical observation and investigation.

Tests for confirming brain death

All brain-stem reflexes should be absent.

(*a*) The pupils are fixed in diameter and do not respond to sharp changes in the intensity of incident light.

(*b*) There is no corneal reflex.

(*c*) The vestibuloocular reflexes are absent. These are absent when no eye movement occurs during or after the slow injection

of 20 ml of ice-cold water into each external auditory meatus in turn, clear access to the tympanic membrane having been established by direct inspection. This test may be contraindicated on one or other side by local trauma.

(*d*) No motor responses within the cranial nerve distribution can be elicited by adequate stimulation of any somatic area.

(*e*) There is no gag reflex or reflex response to bronchial stimulation by a suction catheter passed down the trachea.

(*f*) No respiratory movements occur when the patient is disconnected from the mechanical ventilator for long enough to ensure that the arterial carbon dioxide tension rises above the threshold for stimulating respiration—that is the $Paco_2$ must normally reach 6·7 kPa (50 mm Hg). This is best achieved by measuring the blood gases; if this facility is available the patient should be disconnected when the $Paco_2$ reaches 5·3-6·0 kPa (40-45 mm Hg) after administration of 5% CO_2 in oxygen through the ventilator. This starting level has been chosen because patients may be moderately hypothermic (35°C to 37°C), flaccid, and with a depressed metabolic rate, so that $Paco_2$ rises only slowly in apnoea (about 0·27 kPa/min (2 mm Hg/min)). (Hypoxia during disconnection should be prevented by delivering oxygen at 6 l/min through a catheter into the trachea.)

If blood gas analysis is not available to measure the $Paco_2$ and Pao_2 the alternative procedure is to supply the ventilator with pure oxygen for 10 minutes (preoxygenation), then with 5% CO_2 in oxygen for five minutes, and to disconnect the ventilator for 10 minutes while delivering oxygen at 6 l/min by catheter into the trachea. This establishes diffusion oxygenation and ensures that during apnoea hypoxia will not occur even in 10 or more minutes of respiratory arrest.

Those patients with pre-existing chronic respiratory insufficiency, who may be unresponsive to raised levels of carbon dioxide and who normally exist on a hypoxic drive, are special cases and should be expertly investigated with careful blood gas monitoring.

Other considerations

Repetition of testing—It is customary to repeat the tests to ensure that there has been no observer error. The interval between tests must depend on the primary condition and the clinical course of the disease. Some conditions in which it would be unnecessary to repeat tests since a prognosis of imminent brain death can be accepted as being obvious are listed under the third criteria for considering a diagnosis of brain death (see above). In some conditions the outcome is not so clear-cut and in these the tests should be repeated. The interval between tests depends on the progress of the patient and might be as long as 24 hours. This is a matter for medical judgment, and repetition time must be related to the signs of improvement, stability, or deterioration that present themselves.

Integrity of spinal reflexes—It is well established that spinal cord function can persist after insults that irretrievably destroy brain-stem function. Reflexes of spinal origin may persist or return after an initial absence in brain-dead patients.[4]

Confirmatory investigations—It is now widely accepted that electroencephalography is not necessary for diagnosing brain death.[5-9] Indeed, this view was expressed from Harvard in 1969,[10] only a year after the original Harvard criteria were published. Electroencephalography has its principal value at earlier stages in the care of patients, when the original diagnosis is in doubt. When electroencephalography is used the strict criteria recommended by the Federation of EEG Societies[11] must be followed. Other investigations such as cerebral angiography or cerebral blood flow measurements are not required for diagnosing brain death.

Body temperature—The body temperature in these patients may be low because of depression of central temperature regulation by drugs or by brain-stem damage and it is recommended that it should be not less than 35°C before the diagnostic tests are carried out. A low-reading thermometer should be used.

Specialist opinion and status of doctors concerned—Experienced clinicians in intensive care units, acute medical wards, and accident and emergency departments should not normally require specialist advice. Only when the primary diagnosis is in doubt is it necessary to consult with a neurologist or neurosurgeon. The decision to withdraw artificial support should be made after all the criteria presented above have been fulfilled and can be made by any one of the following combinations of doctors: (*a*) a consultant who is in charge of the case and one other doctor; (*b*) in the absence of a consultant, his deputy, who should have been registered for five years or more and who should have had adequate experience in the care of such cases, and one other doctor.

References

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6 Mohandas, A, and Chou, S N. Brain death. A clinical and pathological study. *Journal of Neurosurgery*, 1971, **35**, 211.

7 Brain damage and brain death. *Lancet*, 1974, **1**, 341.

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9 MacGillivray, B. The diagnosis of cerebral death. In *Proceedings of the Tenth Congress of the European Dialysis and Transplant Association*, ed J F Moorhead. London, Pitman Medical, 1973.

10 Beecher, H K. After the "definition of irreversible coma". *New England Journal of Medicine*, 1969, **281**, 1070.

11 The International Federation of EEG Societies. Report. *Electroencephalography and Clinical Neurophysiology*, 1974, **37**, 430; 1975, **38**, 536.

Do girls achieve nocturnal bladder control before boys? If so, why?

It is said that girls tend to develop bladder control before boys but that at the age of 3 and 4 the numbers of wetters among boys and girls is about equal. Girls also tend to learn to talk before boys. The reasons for these differences are unknown. As for the fact that by the age of 3 or 4 the number of wetters in the sexes is about equal, it is suggested that girls react to stress more at that age, just when they have recently acquired control, and start to wet again. Anyway, the differences are only small.

Is there a rational method of surveillance for people who have had gastrectomies? In what dose and at what intervals should the appropriate replacement treatment be given?

After total gastrectomy the patient is certain eventually to develop vitamin B_{12} deficiency and should begin replacement treatment with monthly injections of 250 mg hydroxycobalamin within a few months of the operation. Absorption of other substances may be impaired, as it is also often after partial gastrectomy. The deficiencies most likely to occur after these operations are of iron, calcium, and vitamin D. One may therefore anticipate such deficiencies by giving supplements to all these patients or, alternatively, rely on annual clinical review with measurements of haemoglobin, serum iron, serum calcium, and alkaline phosphatase concentrations, treating abnormalities as they arise. This policy of surveillance is recommended. If, for reasons of geography, resources, or personality, it is impracticable, regular supplements may be given—for instance, iron by mouth for one week each month. A blunderbuss supplemental tablet is available (Gastrovite (MCP Ltd), which contains ferrous glycine sulphate 225 mg, ascorbic acid, calciferol 200 IU, and calcium gluconate 100 mg), and is likely to be more acceptable to patients than multiple preparations.